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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|--------------------|
| 10/735,174 | 12/12/2003 | Bingsang Huan | NX14C | 4605 |
| 27489 | 7590 | 04/27/2006 | EXAMINER | |
| RALPH T. LILORE 371 FRANKLIN AVENUE THIRD FLOOR - PO BOX 570 NUTLEY, NJ 07110 | | | | HORLICK, KENNETH R |
| | | ART UNIT | | PAPER NUMBER |
| | | | | 1637 |

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/735,174 | HUAN ET AL. | |
| | Examiner | Art Unit | |
| | Kenneth R. Horlick | 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) Claim(s) ____ is/are allowed.
- 6) Claim(s) 1-40 is/are rejected.
- 7) Claim(s) ____ is/are objected to.
- 8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. ____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: ____. |

1. The specification is objected to because of the following informality: the continuation information must be updated to indicate issue of the parent '888 application as U.S. Patent No. 6,696,246.

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,696,246. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims and the instant claims are related as species-genus.

3. Claims 1-40 were previously prosecuted in the parent '888 application. The following rejections are repeated from the Office action mailed 10/25/00.
 4. Applicant is advised that should claims 20-25 & 17, 18, 39 & 40 be found allowable, the claims will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).
Although Claim 20 and 23 recite a different preamble, kit claims are examined on their components. Method claims are examined on their active steps. Claims 20-22 and 23-25 contain the same components. Claims 39 & 40 are recite the same steps of 17 & 18. Appropriate correction is required.
5. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
Claims 20-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 20-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 20-38 are indefinite because of the phrase "essentially complementary". It cannot be determined the degree or by what measure essentially complementary is defined. The metes and bounds of the claims cannot be determined.

B) Claim 12 is confusing. The Markush language recites "and" twice. Typically the last Markush group is recited with "and". It is unclear as to the Markush groupings. It is suggested the first "and" be deleted.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3,5,6,8,10,14-16,19,26,27,31,32 & 34-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Cimino et al (US5,652,096 July 29, 1997).

Cimino et al teach hybridization method for discriminating and partial complementarity between DNA base sequences which is useful in medical diagnostics (see entire doc. esp abstract). They teach that probes containing psoralen may be used to covalently crosslink to targets (see col. 10 lines 16-18 & col. 2 lines 39-60). They also teach attaching a probe to solid

support (bead or membrane) and test multiple different targets such as nucleic acid (see col.12 lines 12-45). In one method they contact probes immobilized to solid support with target nucleic acid containing normal and sickle cell sequence derived from cells. Following photoactivation to induce crosslinking between target and probe, the support is washed and counted to determine amount bound (see example 4). In example 13 they assayed blood samples from human patients for HIV-I. They also teach testing single fragment DNA probed simultaneously probed with two allele specific crosslinkable probes.

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 20-25, 37 & 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino et al (US5,652,096 July 29, 1997).

Cimino et al teach hybridization method for discriminating and partial complementarity between DNA base sequences which is useful in medical diagnostics (see entire doc. esp abstract). They teach that probes containing psoralen may be used to covalently crosslink to targets (see col. 10 lines 16-18 & col. 2 lines 39-60). They also teach attaching a probe to solid support (bead or membrane) and test multiple different targets such as nucleic acid (see col. 12 lines 12-45). In one method they contact probes immobilized to solid support with target nucleic acid contain normal and sickle cell sequence derived from cells. Following photoactivation to induce crosslinking between target and probe, the support is washed and counted to determine amount bound (see example 4). In example 13 they assayed blood samples from human patients for HIV-I. They also teach testing single fragment DNA probed simultaneously probed with two allele specific crosslinkable probes.

Cimino et al do not explicitly teach a kit nor testing a patient sample using immobilized probes.

One of ordinary skill in the art would have been motivated to assay patient samples on Cimino et al's hybridization method using immobilized probes in order to detect pathogens and the disease state of individuals. Cimino et al's method offers greater sensitivity in detection. It would have been prima facie obvious to test patient samples using Cimino et al's method of immobilized probes so that a patient disease state such as HIV status would be detected with increased sensitivity.

Moreover, one of ordinary skill in the art would have been motivated to combine the reagents of Cimino et al hybridization method including probes into a kit in order to provide an efficient and easy handling arrangement to allow a user to perform the method quickly and efficiently. It would have been prima facie obvious to combine all the reagents i.e probe with crosslinking molecule capable of forming a covalent link between probe and target DNA, wash buffer of removing probe not covalently bound and label of Cimino et al's hybridization method into a single kit in order for the practitioner to perform the method conveniently and efficiently.

11. Claims 4, 9, 17, 18, 39 & 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al (Recombinant DNA 2nd edition 1992 pp. 127-130) in view of Cimino et al (US5,652,096 July 29, 1997).

The teachings and suggestions of Cimino et al are described previously.

Cimino et al do not explicitly teach nucleic acids immobilized samples.

Watson et al teach the general method of Northern and Southern blotting whereby nucleic acids are immobilized nitrocellulose filter and probe with labeled probe (see Fig. 7-23).

One or ordinary skill in the art would have been motivated to apply Cimino's hybridization technique to Watson et al's gel blotting in order to increase the accuracy of detection and decrease the hybridization time. Cimino et al state that hybridization methods are time consuming and result in nonspecific binding (see col. 2 lines 20-37). It would have been prima facie obvious to apply Cimino et al's hybridization method to Watson et al's blotting methods in order to detect quickly nucleic acids with greater accuracy.

12. Claims 11-13 & 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino et al (US5,652,096 July 29, 1997) in view of Yabusaki et al (US4,599,303 July 8, 1986).

The teachings and suggestions of Cimino et al are described previously.

Cimino et al do not teach the specific type of claimed crosslinking moieties.

Yabusaki et al teach a method determining the presence of specific nucleic acid base molecules by employing crosslinking reactions of unique molecules capable of forming covalent bonds (see entire document esp abstract). The single stranded DNA or RNA probe is complementary to a unique region of bacterial, viral or mammalian chromosome target sequence. The nucleic acid may be from blood, tissue or cell sample and is reacted with probe under conditions where hybridization of the probe with the target will occur. Following hybridization the sample is subjected to photochemical or chemical procedure which causes cross-linking of the probe to the target sequence. Following crosslinking the uncrosslinked probe is separated using any procedure such as gel filtration, hydroxyapatite chromatography and alkaline hydrolysis etc. The presence is diagnostic for presence of particular viral, bacterial or mammalian target. Detection may be accomplished by incorporation of a radioactive or nonradioactive label (see col. 2 lines 39-66). The cross-linking agent may be psoralens or furocoumarins such as haloalky-coumarins (see col. 5, lines 8-62). Thymidine monadducted to psoralen maybe used (see col. 11 line 65- col.12 line 46).

One of ordinary skill in the art would have been motivated to apply Yabusaki et al's probes to Cimino et al's method of hybridization in order to immobilize either probes or target for detecting DNA sequences. Cimino et al's explicitly suggests that their method may employ Yabusaki et al's described probes (see col.2, lines 39-60) because their crosslinking agents did not inhibit hybridization process and provided suitable bonding. It would have been prima facie obvious to apply Yabusaki et al's probes to Cimino's et al's immobilization onto any commonly used solid support at the time of invention in order to provide a detection assay with high sensitivity (see col.1 lines 45-51).

13. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino et al (US5,652,096 July 29, 1997) in view of Heller et al (US5,849,486 Dec. 15, 1998).

The teachings and suggestions of Cimino et al are described previously.

Cimino et al do not teach using an electric field to desorb non specifically bound nucleic acids.

Heller et al teach a method of using an electric field to remove non specifically bound materials on a matrix array (see abstract and column 11 lines 23-40).

One of ordinary skill would have been motivated to apply Heller et al's teaching of electrically controlled hybridization to Cimino et al's method of covalent crosslinking hybridization in order to increase the discrimination ability of Cimino et al's assay. Heller et al states that electrically controlled hybridization actually enhances the discrimination of assays by eliminating nonspecifically bound materials. It would have been prima facie obvious to apply Heller et al's teachings of electronically controlled hybridization technique to Cimino et al's hybridization method in order to increase assay sensitivity and accuracy in detecting single mismatched hybridizations and even point mutations.

14. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chance et al (US5,645,993 July 8, 1997) in view of Cimino et al (US5,652,096 July 29, 1997).

Chance et al teach immobilizing cell sample on slides for florescence in situ hybridization (see column 9 line 64-66).

Chance et al do not teach crosslinking probes.

The teachings and suggestions of Cimino et al are described previously.

One of ordinary skill would have been motivated to use Cimino et al's method of hybridization on Chance et al's teaching of in situ hybridization on a slide in order to increase

the sensitivity of detection. Cimino et al states that covalent crosslinking increases detection by eliminating non target binding and decreases the incubation time. It would have been prima facie obvious to apply Cimino et al's hybridization techniques to Chance et al's in situ hybridization on a slide in order to increase the detection.

15. No claims are free of the prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R. Horlick whose telephone number is 571-272-0784. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Kenneth R Horlick, Ph.D.

Primary Examiner

Art Unit 1637